

REMARKS

The Official Action of March 31, 2008, and the references cited therein have been carefully considered. The Applicant respectfully requests reconsideration of the application in view of the following remarks.

The claims have been amended consistent with allowable Claim 21 to be directed to compounds wherein Ar is benzisothiazol-3-yl or benzthiophen-3-yl. Applicants preserve the opportunity of pursuing the subject matter wherein Ar is phenyl in a divisional application.

Claims 20-26 have been canceled without prejudice and rewritten for presentation as new Claims 27-31 for convenience in entry of the amendment. Support for this amendment is found in the specification, e.g. pages 4-11, and the claims of the application as filed.

Claims 27-31 are pending in the application.

1. Rejection of Claims 20 and 22-26 for Obviousness over Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al.

Claims 20 and 22-26 stand rejected under 35 U.S.C. § 103(a) as being obvious over Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. The Applicants respectfully traverse this rejection and provide the following comments.

The Applicants respectfully assert that the Examiner has failed to establish a prima facie case of obviousness.

The Applicants respectfully assert that Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. do not disclose or suggest the compounds of the present invention.

The Applicants respectfully assert that Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. would not have motivated one skilled in the art to prepare the compounds of the present invention. The Examiner has failed to demonstrate that Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. would have motivated one of ordinary skill in the art to prepare the compounds of the present invention.

The Applicants respectfully assert that Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. would not have enabled one skilled in the art to prepare the compounds of the present invention. The Examiner has failed to indicate how one of ordinary skill in the art would have been enabled to prepare the compounds of the present invention without undue experimentation based on Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al.

Fletcher and Ackerman et al. and Blurton et al. and Wang disclose a variety of 4-phenylsulfonyl-piperidine compounds that possess e.g., a fluorophenyl or difluorophenyl group.

Patani et al. teaches that bioisosterism is a general approach to drug design. Patani et al. indicate that there are at least 5 different kinds of monovalent bioisosteres: (1) fluorine vs. hydrogen; (2) amino vs. hydroxyl interchanges; (3) thiol vs. hydroxyl interchanges; (4) fluorine, hydroxyl, amino and methyl interchanges; and (5) chloro, bromo, thiol and hydroxyl interchanges.

The compounds disclosed in Fletcher and Ackerman et al. and Blurton et al. and Wang are structurally very different from the presently claimed compounds. In particular, the compounds of the present invention all possess a fluorine substituent adjacent to the phenylsulfonyl group at the 4-position of the piperidine.

None of Fletcher and Ackerman et al. and Blurton et al. and Wang alone or in combination disclose or suggest compounds with a fluorine substituent adjacent to the phenylsulfonyl group at the 4-position of the piperidine.

Applicants respectively submit that there would have been no motivation nor guidance in Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. for one of ordinary skill in the art to have prepared compounds with a fluorine substituent adjacent to the phenylsulfonyl group at the 4-position of the piperidine. The Examiner has not provided any factual basis to support the assertion that Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. would have motivated one of ordinary skill in the art to have prepared the present compounds.

The Examiner agrees that the compounds of the present invention are not "positional isomers" of the compounds of Fletcher and Ackerman et al. and Blurton et al. and Wang.

Applicants respectfully submit that Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. teach away from the present invention by suggesting that a fluorine substituent should be located on a phenyl ring or on a side chain, rather than on the central piperidine ring, in particular, adjacent to the phenylsulfonyl group at the 4-position of the piperidine ring.

Patani et al. teaches that bioisosterism is a general approach to drug design. Patani et al. indicate that there are at least 5 different kinds of monovalent bioisosteres: (1) fluorine vs. hydrogen; (2) amino vs. hydroxyl interchanges; (3) thiol vs. hydroxyl interchanges; (4) fluorine, hydroxyl, amino and methyl interchanges; and (5) chloro, bromo, thiol and hydroxyl interchanges.

Patani et al. does not remedy the deficiencies of Fletcher and Ackerman et al. and Blurton et al. and Wang alone or in combination. Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. would not have suggested compounds with a fluorine substituent adjacent to the phenylsulfonyl group at the 4-position of the piperidine. Nothing in Patani et al. suggest that a fluorine substituent should be inserted adjacent to the phenylsulfonyl group at the 4-position of the piperidine in the compounds of Fletcher and Ackerman et al. and Blurton et al. and Wang.

Based on Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. there would have been e.g.: no direction for one of ordinary skill in the art to select fluorine over any other substituent; no direction regarding which of the numerous hydrogen atoms should be replaced with a fluorine; no direction regarding which of the 9 available hydrogen atoms on the piperidine ring should be replaced with a fluorine; no direction regarding which position on piperidine ring should be substituted with a fluorine; and no direction regarding how many fluorine groups should have been included on the piperidine ring.

Even if one of ordinary skill in the art had been motivated to alter the compounds of Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al., there would have been no direction in Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. regarding how such compounds could have been prepared without undue experimentation. There is no teaching in Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. regarding how to put a fluoro group on the piperidine ring at all, let alone at the bridgehead position adjacent to the phenylsulfonyl group.


Accordingly, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness and that the rejection of Claims 20 and 22-26 under 35 U.S.C. § 103(a) as being obviousness over Fletcher and Ackerman et al. and Blurton et al. and Wang, in view of Patani et al. is untenable and should be withdrawn. In view of the present amendment to direct the claims to compounds wherein Ar is benzisothiazol-3-yl or benzthiophen-3-yl and to cancel the subject matter wherein Ar is phenyl, this rejection has been rendered moot.

2. Allowable Subject Matter

Applicants gratefully acknowledge that Claim 21 would be allowable if put in proper dependent form. In view of the amendments and remarks above to direct to the main independent Claim 27 to definitions of Ar wherein Ar is benzisothiazol-3-yl or benzthiophen-3-yl, all of the remaining claims should also be allowable because they depend from or otherwise incorporate the limitations of the main claim.

Applicants respectfully contend that the application is allowable and a favorable response from the Examiner is earnestly solicited.

Respectfully submitted,

By   
J. Eric Thies  
Reg. No. 35,382  
Attorney for Applicant

MERCK & CO., Inc.  
P.O. Box 2000  
Rahway, New Jersey 07065-0907  
(732) 594-3904

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